C-3405/0/US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Hageman, M.J. *et al.*	ATTORNEY DOCKET NO.:	C-3405/0/US
SERIAL NO.:	09/730,663	GROUP ART UNIT:	1626
FILED:	December 6, 2000	EXAMINER:	G.M. Shameem

TITLE: SOLID STATE FORM OF CELECOXIB HAVING ENHANCED BIOAVAILABILITY

DATE: December 2, 2002

CERTIFICATE OF MAILING

I hereby certify that this document and its listed enclosures are being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC 20231 on (date) December 2, 2002.

Susan B. Gaulik

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PETITION FOR EXTENSION OF TIME UNDER 37 CFR §1.136(a)

Applicant hereby requests an extension of time of three months in which to respond to the Office Action dated June 7, 2002 in the above identified Application. That Office Action set a shortened statutory period of three months for response. Please charge $920 or the fee required under 37 CFR §1.17(a)(3) to Deposit Account No. 19-1025.

RESPONSE TO OFFICE ACTION DATED JUNE 7, 2002

Claims 1 and 15 are pending in the above-identified Application and stand rejected under 35 USC §103(a) as being unpatentable over U.S. Patent No. 5,466,823 (Talley).

The Examiner cites *In re Weijlard*, 69 USPQ 86 (CCPA 1946) in support of his position that "there is no patentable distinction in the concept of a chemical compound in crystalline form over the same compound [in] its amorphous form" (Office Action, p. 3, 1st para.). In this regard, Applicant notes that the full context of the referenced remark in *In re*

Weijlard reads as follows:

> "It has long been the practice in the chemical and pharmaceutical arts to produce compounds in the form of crystals to secure a pure product and for other reasons. In this case we see no patentable distinction between the crystalline compound defined in the claims and the substantially pure amorphous product of the reference. In arriving at this conclusion the relative hygroscopicity of the two forms has not been overlooked, but it is our opinion that there is nothing whatever patentable in the concept of a chemical compound in crystalline form over the same compound in its amorphous form."

Emphasis added.

The *Weijlard* court's finding of "no patentable distinction" was therefore in a fact situation where the amorphous form was in the prior art and the crystalline form was new, and where crystallization was standard practice in the art. In the present situation, the facts are reversed. Crystalline celecoxib is old in the art (as disclosed for example in the Talley reference) and the present invention goes against the teaching of Talley to provide amorphous celecoxib.

Even if it were obvious, as the court in *In re Weijlard* found, to proceed from an amorphous to a crystalline form of a compound, the Examiner has failed to make a *prima facie* case of obviousness for proceeding from the crystalline celecoxib of Talley to the amorphous celecoxib of the present invention.

In particular, no suggestion or motivation to modify Talley's crystalline celecoxib to make amorphous celecoxib is found either in Talley itself or in the knowledge generally available to one of ordinary skill in the art at the time the invention was made. See MPEP 2143, first para. It was not even predictable that an amorphous form of celecoxib could exist or be made. "Certain materials are easy to cast into a glassy [*i.e.*, amorphous] state, others can be made glassy with great difficulty and, some, seemingly not at all. At present there seems to be no specific theory to help predict this behavior." Remington: The Science and Practice of Pharmacy, 19th edition (1995), p. 168 (copy attached). At least some degree of predictability is required for a *prima facie* showing of obviousness. MPEP 2143.02, second subsection. Thus the Examiner's assertion that "one skilled in the art would have been motivated to prepare different amorphous forms of known pharmaceutically useful compounds with the expectation of obtaining a pharmaceutically useful benefit, such as treating a medical

condition or disorder" is incorrect. Such an assertion, in a situation where, because of lack of predictability, there was no reasonable expectation of success at the time the invention was made, can be made only with the benefit of hindsight, which is impermissible. Further, it is respectfully pointed out that the present invention did not involve preparing "different amorphous forms" but in preparing for the first time an amorphous form where only crystalline forms were known in the art.

Even if, *arguendo*, a *prima facie* case of obviousness had been made, evidence exists to rebut it. The Examiner correctly notes that in *Ex parte Conn & Norman*, 119 USPQ 388 the Board of Patent Appeals and Interferences, quoting *Union Carbide v. American Carbide*, 181 F 104, stated that mere change of form in and of itself does not disclose novelty. The court in *Union Carbide* went on to say:

> "... But patentable novelty in a case like the present may be founded upon superior efficiency; upon superior durability, including the ability to retain a permanent form when exposed to the atmosphere; upon a lesser tendency to breakage and loss; upon purity, and, in connection with other things, upon comparative cheapness."

The Board in *Ex parte Conn & Norman* found that a similar situation to that in *Union Carbide* presented itself, "because the advantages afforded by the claimed compound stem from its new form. Since this form of the compound is neither taught nor suggested in the prior art, its novelty coupled with the unobvious results obtained thereby renders it patentable."

The citation of *Ex parte Conn & Norman* in the present Office Action is followed by a statement that "absent a showing of unobvious and superior properties, the instant claimed amorphous forms of a known compound would have been suggested to one skilled in the art."

Although, where a *prima facie* case of obviousness has not been made, there is no burden on Applicant to provide a showing of unobvious and superior properties, Applicant respectfully draws the Examiner's attention to the present specification at page 31, Table 3. In a pharmacokinetic study in dogs, a tablet comprising amorphous celecoxib of the invention exhibited an approximately twofold higher C_{max} and an approximately twofold higher AUC, *i.e.*, a doubling of bioavailability, by comparison with a prior art capsule comprising crystalline celecoxib. Furthermore, a blood plasma celecoxib level of 1011 ng/ml, reached in 1.2 hours with the prior art crystalline form, was reached in just 0.5 hour with the amorphous form of the invention. Such a quantitative improvement in bioavailability could not possibly have been

expected, and constitutes evidence of just the kind of "unobvious and superior properties" that the Examiner implies is absent.

Ex parte Hartop, 139 USPQ 525 is cited by the Examiner in support of his statement that "products which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable where products have same utility as the art compounds." The Board in *Ex parte Hartop* continued:

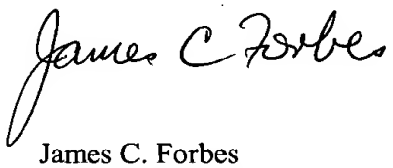
"... however, invention can be present if prior art product cannot be used for purpose asserted for pure or new form of product."

It was an objective of the present invention to provide a form of celecoxib capable of providing rapid-onset therapeutic effect, for example fast relief from acute pain. Specification, page 2, lines 4–10. Crystalline celecoxib presents certain problems, mentioned in the specification at page 2, lines 11–25, in preparing a rapid-onset oral dosage form. Talley, at column 4, lines 30–33, contemplates that his subject compounds, including celecoxib, "would be useful ... as an analgesic in the treatment of pain and headaches" but does not specifically suggest utility in rapid-onset therapy, such as for fast relief from acute pain.

The present invention provides a previously unknown solution to the problem of providing a form of celecoxib having enhanced bioavailability consistent with rapid-onset therapy; furthermore, as shown in Table 3 of the specification as pointed out above, it does so to a most surprising degree.

Accordingly Applicant respectfully traverses the present rejection under 35 USC §103(a) and believes that the claims presently in consideration are in condition for allowance.

Respectfully submitted,



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Enclosures:
Fee Transmittal Sheet
Cited document: Remington (1995) p. 168

PTO/SB/17 (11-00)
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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2001

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT	$920.00

Complete if Known	
Application Number	09/730,663
Filing Date	December 6, 2000
First Named Inventor	Hageman, M.J.
Examiner Name	G.M Shameem
Group Art Unit	1626
Attorney Docket No.	C-3405/0/US

METHOD OF PAYMENT

1. ☐ The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number: **19-1025**

Deposit Account Name: **Pharmacia Corporation**

☒ Charge Any Additional Fee Required Under 37 CFR §§ 1.16 and 1.17

☐ Applicant claims small entity status. See 37 CFR § 1.27

2. ☐ Payment Enclosed:

☐ Check ☐ Credit card ☐ Money Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	710	201	355	Utility filing fee	
106	320	206	160	Design filing fee	
107	490	207	245	Plant filing fee	
108	710	208	355	Reissue filing fee	
114	150	214	75	Provisional filing fee	
				SUBTOTAL (1)	

2. EXTRA CLAIM FEES

	Extra Claims			Fee from below		Fee Paid
Total Claims		-20** =	0	X	=	0.00
Independent Claims		- 3** =	0	X	=	0.00
Multiple Dependent					=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	80	202	40	Independent claims in excess of 3
104	270	204	135	Multiple dependent claim, if not paid
109	80	209	40	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent
				SUBTOTAL (2) $0.00

***or number previously paid, if greater; For Reissues, see above*

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non - English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	390	216	195	Extension for reply within second month	
117	890	217	445	Extension for reply within third month	920.00
118	1,390	218	695	Extension for reply within fourth month	
128	1,890	228	945	Extension for reply within fifth month	
119	310	219	155	Notice of Appeal	
120	310	220	155	Filing a brief in support of an appeal	
121	270	221	135	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,240	241	620	Petition to revive - unintentional	
142	1,240	242	620	Utility issue fee (or reissue)	
143	440	243	220	Design issue fee	
144	600	244	300	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR § 1.17(q)	
126	180	126	180	Submission of Information Disclosure Statement	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	710	246	355	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	710	249	355	For each additional invention to be examined (37 CFR § 1.129(b))	
179	710	279	355	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	
Other fee (specify)					

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) $920.00

SUBMITTED BY

Complete *(if applicable)*

Name (Print/Type)	James C. Forbes	Registration No. (Attorney/Agent)	39,457	Telephone	847-581-6090
Signature	James C Forbes			Date	December 2, 2002

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